| Pfizer Inc. | CP-601927 |
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| **Mechanism of Action** | Nicotinic acetylcholine receptor α4β2 (α4β2 nAChR) partial agonist<br>http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=465&familyId=76<br>http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=472&familyId=76<br>http://www.ncbi.nlm.nih.gov/gene/1137; http://www.ncbi.nlm.nih.gov/gene/1141 |
| **Overview** | CP-601927 is a CNS-penetrant, high affinity, selective (> 39-fold affinity relative to other nAChRs and no biologically-significant secondary pharmacodynamic interactions, as assessed in a broad *in vitro* binding screen), partial agonist at the a4b2 nAChR. |
| **Safety/Tolerability** | CP-601927 was generally safe and well tolerated in doses up to 2 mg BID in nonsmokers. Based on the pharmacologic properties of CP-601927, the toxicologic findings, and previous human experience, the primary potential risks to humans are nausea, vomiting, dizziness, insomnia, somnolence, abdominal pain, headache, vertigo, irritability, dyspepsia, and liver enzyme elevation.<br><br>Nonclinical toxicology data support clinical studies up to 6 weeks in duration. |
| **Additional Information** | In a SPECT study in recreational smokers, CP-601927 displaces [123I]5-I-A-85380, a ligand of brain a4b2 nAChRs following a 1 or 3 mg dose of CP-601927. The displacing effect of CP-601927 appears to be comparable to that of nicotine dosed as a 7 mg/day patch.<br><br>CP-601,927 did not demonstrate efficacy in a 4 week study in attention deficit hyperactivity disorder (ADHD) or in a smoking cessation study. |
| **Suitable for and Exclusions** | Clinical trials of up to 6 weeks duration with careful monitoring of hepatic function and for evidence of suicidality. |
| **Clinical Trials** | http://www.clinicaltrials.gov/search?term=%22CP-601,927%22 |
| **Publications** | http://onlinelibrary.wiley.com/doi/10.1002/bdrb.20298/full<br>http://dx.doi.org/10.1016/S0016-5085(09)62444-6<br>http://www.ncbi.nlm.nih.gov/pubmed?term=CP-601%2C927 |